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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/071,829	02/07/2002	Mark Douglas Howell	704613-5001	4144

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EXAMINER	
LAM, ANN Y	

ART UNIT	PAPER NUMBER
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/071,829	HOWELL ET AL.	
	Examiner	Art Unit	
	Ann Y. Lam	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *50-87* is/are pending in the application.

4a) Of the above claim(s) *75-79,82 and 87* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *50-74,80,81 and 83-86* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *4/29/027 February 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 21, 2007 has been entered.

Status of Claims

Claims 1-49 are cancelled.

Claim 75-79, 82 and 87 are withdrawn.

Claims 50-74, 80-81, 83-86 are examined below.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent

granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

1. Claims 50, 51, 60, 61, 69-74 are rejected under 35 U.S.C. 102(e) as being anticipated by Lentz, 6,620,382, in light of Ebach et al., "Opposing effects of tumor necrosis factor receptor 1 and 2 in sepsis due to cecal ligation and puncture", Shock, 2005 April; 23(4):311-8 .

As to claim 50, Lentz teaches a device for reducing the amount of a targeted immune system inhibitor in blood, comprising

an absorbent matrix comprising an inert medium attached to at least one binding partner capable of specifically binding to a targeted immune system inhibitor (see col. 6, lines 41-51, which discloses that TNF receptor 1 and TNF receptor 2 molecules are removed using antibody immunoreactive against the receptor molecules, the antibodies being immobilized on the ultrapheresis membrane—the ultrapheresis membrane is considered the claimed inert medium and the antibody is considered the claimed binding partner),

and a conduit (18, col. 3, lines 59-60 and fig. 1) for conducting the blood to the absorbent matrix to produce altered blood having a reduced amount of the targeted immune system inhibitor (see col. 3, lines 53-60 and col. 4, lines 1-4),

wherein all of said binding partners in said extracorporeal system are binding partners to soluble receptors for tumor necrosis factor alpha (col. 6, lines 41-42). (Examiner notes that Applicant's claims are interpreted as if the receptor for tumor necrosis factor alpha and the receptor for tumor necrosis factor beta are two separate

species in the Markush group.) While Lentz discloses that TNF receptor 1 and TNF receptor 2 molecules are removed using antibodies (col. 6, lines 41-47), Lentz does not explicitly disclose that TNF receptor 1 and TNF receptor 2 are receptors for TNF-alpha, Ebach et al. teach that this is the case. Ebach et al. teach that TNF-alpha binds to two distinct receptors : TNF receptor 1 and TNF receptor 2 (see abstract). Thus Ebach et al. teach that TNF receptor 1 and TNF receptor 2 are receptors for TNF-alpha. (The receptors are also soluble, being in a fluid sample, i.e., blood—see Lentz, col. 8, line 33).

As to the following claims, Lentz discloses the limitations as follows.

As to claim 51, the targeted immune system inhibitor is present in a plasma component of the blood (col. 8, line 33.)

As to claim 60, the binding partner is a binding partner to which the targeted immune system inhibitor binds to in nature, or a fragment of the binding partner to which the targeted immune system inhibitor binds to in nature, wherein the fragment specifically binds to the targeted immune system inhibitor (col.6, lines 41-49.)

As to claim 61, the binding partner or fragment is produced recombinantly (col. 6, line 48).

As to claims 69 and 73, the binding partner is produced synthetically (col. 6, line 48).

As to claims 70 and 72,the synthetic peptide is conjugated to a carrier (col. 6, line 50.)

As to claims 71 and 74, the binding partner comprises a plurality of synthetic peptides capable of specifically binding to the targeted immune system inhibitor (col. 6, lines 50.)

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 62-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lentz, 6,620,382, in light of Ebach et al., "Opposing effects of tumor necrosis factor receptor 1 and 2 in sepsis due to cecal ligation and puncture", Shock, 2005 April; 23(4):311-8, and in view of Greenblatt, et al., "The type B receptor for tumor necrosis factor-.alpha. mediates DNA fragmentation in HL-60 and U937 cells and differentiation in HL-60 cells", Blood, 1992, pp. 1339-46, Vol. 80.

Lentz in light of Ebach et al. teaches the invention substantially as claimed (see above with respect to claim 50). While Lentz teaches that the antibodies to the TNF receptor 1 and TNF receptor 2 molecules may be single chain, recombinant or humanized, Lentz does not specifically teach that the antibodies are monoclonal (as recited in claims 62-65)..

However, Greenblatt et al. teach that monoclonal antibodies against the receptor for tumor necrosis factor alpha are known (see abstract.) It would have been obvious to one of ordinary skill in the art to provide antibodies against the receptor for tumor necrosis factor alpha that are monoclonal antibodies in the Lentz apparatus because Lentz teaches use of antibodies to removed receptors to tumor necrosis factor receptors in general and one would use the appropriate reagent, in this case the antibody of Greenblatt, to remove the desired analytes. Because Lentz suggests that various types of antibodies against the receptor for tumor necrosis factor alpha may be used (see col. 6, lines 45-48), one of ordinary skill in the art would have reasonable expectation of success in utilizing the monoclonal antibodies taught by Greenblatt et al. in the Lentz apparatus.

As to claim 63, Greenblatt teaches that the antibodies are produced recombinantly (see page 1339, right col., last partial paragraph).

As to claim 64 and 65, the binding partner comprising a plurality of different monoclonal antibody preparations capable of specifically binding to a plurality of targeted immune system inhibitors (Lentz teaches a plurality of antibodies on an immunosorbent, see column 6, line 50, and Greenblatt teaches the monoclonal antibody claimed.)

3. Claims 66-68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lentz, 6,620,382, in light of Ebach et al., "Opposing effects of tumor necrosis factor receptor 1 and 2 in sepsis due to cecal ligation and puncture", Shock, 2005 April;

23(4):311-8, and in view of Yelavarthi et al., "Analysis of p60 and p80 tumor necrosis factor-.alpha", American Journal of Pathology, 1993, pp. 1131-41, Vol. 143.

Lentz in light of Ebach et al. teaches the invention substantially as claimed (see above with respect to claim 50), except for the antibodies against the receptor for tumor necrosis factor alpha being polyclonal.

However, Yelavarthi teaches that polyclonal antibodies against the receptor for tumor necrosis factor alpha are known (see Yelavarthi abstract disclosing that "[t]ranslation was verified in all samples by immunohistology using polyclonal antibodies specific for the receptor proteins.")

It would have been obvious to one of ordinary skill in the art to utilize the antibody against the receptor for tumor necrosis factor alpha taught by Yelavarthi as the antibody binding partner in the Lentz invention because Lentz teaches removal of receptors to tumor necrosis factor receptors in general and one would use the appropriate reagent, in this case the antibody of Yelavarthi to remove the desired analyte.

As to claims 66, the Yelavarthi antibody is a binding partner to which the targeted immune system inhibitor binds to in nature, or a fragment of the binding partner to which the targeted immune system inhibitor binds to in nature, wherein the fragment specifically binds to the targeted immune system inhibitor (see Yelavarthi abstract.)

As to claims 67 and 68, the binding partner comprising a plurality of different polyclonal antibody preparations capable of binding to a plurality of targeted immune system inhibitors (Lentz teaches a plurality of antibodies on an immunosorbent, see column 6, line 50, and Yelavarthi teaches the polyclonal antibody claimed.)

4. Claims 52-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lentz, 6,620,382, in light of Ebach et al., "Opposing effects of tumor necrosis factor receptor 1 and 2 in sepsis due to cecal ligation and puncture", Shock, 2005 April; 23(4):311-8, and in view of Prusiner et al., 6,221,614.

Lentz in light of Ebach et al. teaches the invention substantially as claimed (see above with respect to claim 50.)

While Lentz teaches that the antibodies are immobilized on a membrane (i.e., the claimed inert medium), Lentz does not teach that medium may be a hollow fiber (as recited in claim 53), a cellulose-based fiber (claim 55), a synthetic fiber (claim 56), or a flat membrane (claim 57), or a bead (claim 54), or a silica-based particle (claims 52 and 58), or that the binding partner is covalently joined to an inert medium (claim 59).

However, Prusiner teaches these limitations by teaching an extracorporeal device to remove material from blood through complexing with an immobilized agent on a support (col. 8, lines 42-51), wherein the immobilized agent may be an antibody (col. 15, lines 37-38.) Prusiner further teaches that the support may be of various types, such as a membrane, which may be in planar form, in the form of hollow fibers , or in the form of flat foils (col. 13, lines 48-50), and that suitable materials for the membrane include cellulose, acrylic copolymer (col. 13, lines 48-56.) Prusiner teaches that the support should have good flow characteristics and low compressibility under clinical flow rates in a particular range (col. 13, lines 65-67). The support may also be silica beads as they are useful as support material (col. 12, lines 41 and 50-52).

It would have been obvious to one of ordinary skill in the art to provide a hollow fiber, cellulose-based fiber, or flat membrane or silica beads as taught by Prusiner as the solid support generally disclosed by Lentz because Prusiner teaches supports made of these various forms and materials are suitable for immobilizing antibodies and also suggest that they can provide the benefit of providing good flow characteristics and low compressibility as would be desirable for clinical purposes.

As to claim 56, the fiber may be produced synthetically. (Examiner notes that Applicant claims that the fiber is a synthetic fiber. However, since Applicant is claiming a device, the claim is interpreted as if it was a product-by-process claim. Thus, the prior art meets the claim since the fiber may be produced synthetically.)

Moreover, as to claim 59, Prusiner teaches that the safest coupling between a complexing agent and a membrane is covalent coupling, which depends on the choice of membrane material and the nature of the complexing agent (col. 15, lines 58-67.)

It would have been obvious to one of ordinary skill in the art to provide in the Lentz membrane, a complexing agent that would allow for covalent coupling as taught by Prusiner because Prusiner teaches that such an agent provides the benefit of safe coupling.

5. Claims 80, 81, 83-86 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lentz, 6,620,382, in light of Ebach et al., "Opposing effects of tumor necrosis factor receptor 1 and 2 in sepsis due to cecal ligation and puncture", Shock, 2005 April; 23(4):311-8, and in view of Imaizumi et al., GB 1,562,546.

Lentz in light of Ebach et al. disclose the invention substantially as claimed (see above with respect to claim 50 regarding the membrane with antibodies for binding to receptors for tumor necrosis factor alpha—the membrane is considered the claimed means for providing a binding partner).

However, with respect to claims 80, 81, 83-86, Lentz does not teach a means for separating whole blood into cellular component and acellular component, a means for conducting the acellular component to the means for providing a binding partner capable of specifically binding to the targeted immune system inhibitor, nor a means for conducting the altered acellular component to the cellular component to produce an altered whole blood.

However, Imaizumi et al. disclose these limitations by disclosing a device comprising an inlet, a separating means connected to the inlet and having a single filter membrane for separating plasma from recirculating blood, an adsorber connected to the filter means and having an adsorbent, such as antibodies, to remove from the separated plasma specific factors for clinical purposes, and means for remixing the plasma from which the specific factors have been removed with the blood from which the plasma has been separated, and an outlet for the recirculating remixed blood (see page 2, lines 31-52). Imaizumi et al. teach that removal of specific factors from blood with remarkably improved efficiency can be achieved by providing a filter before an adsorber in an apparatus wherein the plasma in blood circulating externally of the body is separated by the filter from the blood cells comprising red blood cells, white blood cells and platelets

and is treated in the adsorber with adsorbent comprising antibodies, for example (page 1, lines 71-85.)

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the Lentz apparatus to include a filter before the absorber with antibodies wherein the plasma in blood is separated by the filter from the blood cells, as taught by Imaizumi et al., because Imaizumi et al. teach that the filter provides the advantage of achieving remarkably improved efficiency of removal of specific factors from blood.

Response to Arguments

Applicants' arguments filed March 28, 2006 have been considered. In view of the amendments to the claims, the 112, second paragraph rejections are hereby withdrawn.

Applicants request clarification regarding the rejections because Ebach's publication date in 2005 is roughly three years after Applicants' filing date.

In response to Applicants' request for clarification, Examiner notes that the grounds for rejections do not rely on Ebach to teach or suggest the disclosed invention, but rather to provide evidence of an inherency in the disclosure by Lentz. As indicated above, while Lentz does not explicitly disclose that TNF receptor 1 and TNF receptor 2 are receptors for TNF-alpha, Ebach et al. teach that this is the case. Ebach et al. teach that TNF-alpha binds to two distinct receptors : TNF receptor 1 and TNF receptor 2 (see abstract). Thus Ebach et al. teach that TNF receptor 1 and TNF receptor 2 are receptors for TNF-alpha. Thus, since the Ebach et al. disclosure is used only to provide

evidence of an inherency in the disclosure by Lentz, the Ebach et al. reference does not need to antedate Applicants' filing date.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ann Y. Lam whose telephone number is 571-272-0822. The examiner can normally be reached on Mon.-Fri. 10-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ANN YEN LAM
PATENT EXAMINER